In 41 (28.1%) of the illnesses investigated, one or more pathogens were isolated from throat swabs.

Nineteen isolations of Coxsackie B3 virus and one of Coxsackie B4 virus were made over a period of 12 weeks during the summer of 1958. Most patients suffered from a febrile pharyngitis, but two myalgic and one mild meningeal illness also occurred. This epidemic coincided with an increased prevalence of Coxsackie B3 virus infection in West Surrey.

Four adenoviruses of types 1 to 4 inclusive were isolated, associated with three illnesses characterized by pharyngitis and lymphadenopathy and one by pharyngoconjunctivitis.

Str. pyogenes was isolated 18 times. Pharyngitis more severe than that seen in any other illnesses at the time, with some involvement of the upper respiratory tract, characterized these infections.

Though the frequency distribution of particular symptoms varies to some extent in the different infections, it is clear that in the individual patient a clinical diagnosis of the infecting agent cannot be made with certainty. Further knowledge of the aetiology of these upper respiratory infections can come about only by close collaboration of the medical practitioner with the laboratory.

During the investigation, typing of Coxsackie B viruses and adenoviruses was kindly carried out by Dr. A. J. H. Tomlinson, Bacteriological Laboratory, County Hall, London, and by the Virus Reference Laboratory, Colindale. We are also grateful to Dr. N. Richardson, Pathological Laboratory, Epsom District Hospital, for organizing facilities for storage and transport of frozen specimens; and to the Distillers Company Limited, Great Burgh, Epsom, for supplies of "cardice."

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Requirements for Halsted's mosquito artery forceps (stainless steel, nominal overall length 4¼ in.) are specified in a new British Standard (B.S. 3246:1960). Copies of this standard may be obtained from the British Standards Institution, Sales Branch, 2, Park Street, London, W.1. Price 4s. (Postage extra to non-subscribers.)

IS UNIVERSAL VACCINATION AGAINST PERTUSSIS ALWAYS JUSTIFIED?

BY

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Pertussis is still a great child-killer in many countries. Effective vaccines are now available, but are not devoid of risks, especially of a neurological nature. In some countries—for example, Sweden—the illness has assumed increasingly mild forms and the mortality is now very low. Thus the situation may arise when we must weigh up the relative advantages and disadvantages of vaccination.

There is no doubt that the new vaccines are very effective against pertussis. The British Medical Research Council reported in 1951 that cases of pertussis had been reduced to about one-fifth. Similar results are reported from the U.S.A. The new Swedish pertussis vaccine, which is given as a triple-vaccine (alum-precipitated) against diphtheria, tetanus, and whooping-cough, is prepared on modern principles (Arvidson and Ullberg-Olsson, 1952). It has good serological action (Ericsson *et al.*, 1952; Vahlquist *et al.*, 1954; Laurell *et al.*, 1957). The effect of its application to the community compares favourably with that produced by the best foreign vaccines (Rabo, 1956).

Neurological Complications after Pertussis Vaccination

The earliest report of neurological complications after pertussis vaccination came from Denmark (Madsen, 1933). Other isolated instances were published later, but the first really alarming report came from the U.S.A. when Byers and Moll (1948) described 15 severe cases; two of the patients died. All of those who recovered showed persistent convulsions, seven were mentally retarded, five had a hemiplegia, and two were blind. Toomey (1949) thereafter addressed a questionary to paediatricians in the U.S.A.; 54 answered and reported 38 cases of convulsions with 2 deaths and 12 irreversible cerebral lesions. In Switzerland, Köng (1953), who had himself observed one death and one case of convulsions accompanied by hemiplegia, reported 82 cases known up to 1951. Halpern and Halpern (1955) sent out a new questionary in the U.S.A., and received 56 replies reporting 15 cases of convulsions with one death and three irreversible lesions. Relatively speaking, the situation appeared to have improved, and this was attributed to the higher degree of purity of the vaccines.

In 1958 Berg reported on a personally observed case (convulsions and progressive dementia), which was the seventh from Great Britain. Berg collected data on 108 cases. Many different types of vaccine were implicated; the reactions might occur after any of a series of inoculations, but were more common after the first or second; the interval between vaccination and onset of reactions was usually brief. There were 15 deaths. Thursby-Pelham and Giles (1958) reported six cases (one of which had been included in Berg's series), Andrews (1958) two, and Leigh (1958) and Jones (1958) one each.

Soon after the introduction of triple vaccination on a large scale in Sweden in the mid-'fifties, suspect cases of severe vaccination reactions came to our knowledge. Consequently, at the end of 1958 a questionary was addressed to all 36 children's hospitals and to all 28

hospitals for infectious diseases; replies were received in every case. Subsequently questionaries were sent to 693 child-welfare centres asking for reports on unusual cases observed among out-patients. Replies were received from 559 (81%).

Neurological complications among in-patients during the years 1955–8 were reported in 18 cases. There were four deaths, two of which were sudden. One child was found dead in bed 20 minutes after the second injection; the other, six hours after the first inoculation. In the third fatal case the child developed fever and showed great anxiety after the second injection. Thereafter the child became comatose and later developed convulsions and paresis of the ocular muscles and left arm. Death occurred on the fifth day. Histological examination of the brain showed signs of an acute encephalitis with perivascular infiltration and demyelination. The fourth fatal case showed symptoms of mild rhinopharyngitis one day after the third injection. Severe convulsions developed on the fourth day, and the child died suddenly on the fifth day. In this case histological examination of the brain showed small ring haemorrhages and perivascular oedema with some cellular infiltration.

Of the 14 children who survived, three developed a decerebrate condition. The first of these was feverish, vomited, and had screaming fits for several days after the second inoculation. Thereafter there was progressive mental deterioration. The same acute condition, combined with convulsions, rigidity, conjugate deviation of the eyes, and nystagmus, came on in the second child after the first inoculation. The third case had fever for two to three days after the first injection and was listless for a week; after the second injection there was a similar reaction, but on this occasion it was followed by convulsions and rapid mental deterioration.

In the remaining 11 cases the predominant signs in the acute stage consisted of convulsions in six cases, stupor and coma in three, and collapse in one case. These signs developed from two to three hours after the injection up to five and seven days. The eleventh patient showed marked listlessness after the first two inoculations and increasing mental deterioration after the third. Five of these patients were fully restored to health. Mental retardation was seen in three patients, in one combined with cerebral palsy and deafness, and in another with cerebral palsy and epilepsy. In the remaining three patients epilepsy developed in one case immediately (a mongoloid child), in the others after one and three months.

Neurological complications among patients at the welfare centres were observed in two cases in 1955, in five cases in 1957, and in 11 cases in 1958, making 18 in all. Fifteen of these patients had convulsions, two became comatose, and one had a "collapse." Convulsions were reported in one case after all three injections and in another after two. Repeated attacks after one injection were seen in three patients. Fever was a usual symptom. The time interval in eight cases was 3–12 hours, in four cases 12–24 hours; one started to react on the second day and one on the fifth.

To summarize, a total of 36 children showed neurological manifestations. In 24 of these the initial symptom was convulsions, in six cases coma, and in four acute collapse. At least 11 and probably 13 children had signs indicative of an encephalopathy. Altogether there were four deaths. Of those who recovered, nine showed severe cerebral sequelae.

Comparison Between Neurological Complications after Pertussis and after Pertussis Vaccination

Byers and Moll (1948) reported 26 severe pertussis encephalopathies during 10 years at the hospital in Boston where their 15 examples of post-vaccination lesions were observed. It is unfortunate that these figures cannot be correlated with the incidence of the disease or the total number of vaccinations.

Some idea of the incidence of neurological reactions to pertussis can be obtained from material collected during the 10-year period 1948–57 from the 64 hospitals in Sweden previously mentioned. During those years 31 children with neurological complications to pertussis were treated in these hospitals. Of these children, two died and eight had severe sequelae with cerebral palsy, mental retardation, or epilepsy. A rough calculation shows that during this 10-year period about 725,000 children in Sweden had developed pertussis. During 1955–8 17 examples of cerebral complications after vaccination had been treated in the same hospitals. During the same period roughly 215,000 children had been vaccinated at the child-welfare centres.

With due reservation for the problems involved in diagnosis and in the collection of the material, and for the approximations in the calculation, it might be fair to say that in Sweden the incidence of neurological complications after pertussis does not appear to be as high as that after vaccination. The total incidence of neurological reactions after vaccination in the present series was 36 in a total of 215,000 vaccinated children, or about 1 in 6,000; death or permanent defect occurred in 13, or about 1 in 17,000.

Pertussis Morbidity and Mortality in Sweden

Reports of susceptibility to pertussis vary fairly considerably—Sako (1950) 80–90%, de Rudder (1934) 60–80%, Bradford (1952) 85–90%, Smillie (1952) 95%. A distinction should perhaps be made between "susceptibility to the infection" and the disease in its distinctive and manifest form. "Clinical whooping-cough"—that is to say, with typical attacks—accounts, according to Gordon and Hood (1951), for 75% of cases or above.

To assess the morbidity in Stockholm, I made a study of the records of 2,000 schoolchildren born in 1939 whose detailed clinical records were available up to 1951—that is, up to an age of 12 or 13 years. The number who had developed recognizable pertussis was 1,331 (65%). In the highest social class the figure was 69%, in the lowest 62%. Thus Stockholm seems to have a comparatively low morbidity.

The mortality from pertussis in Sweden, as in other countries, has dropped very greatly in recent years. Thus in the five-year period 1911–15 nearly 800 children died each year from pertussis, against only 10 in the period 1951–5. Indeed, even among infants the mortality is now very low. Among hospitalized patients in Stockholm, for example, the mortality during the period 1934–53 had fallen from 3.4% to zero (Jernelius, 1958).

The fall in mortality is undoubtedly due in large part to the general improvement in children's health and to the improvement in social and medical facilities. A similar reduction of mortality has taken place in other contagious diseases, such as measles and scarlet fever.

Survey of Neurological Reactions after Pertussis Vaccination

Adding to Berg's figure from 1958 the cases reported in Great Britain and in this study, the total of 153 cases is distributed as follows: U.S.A. 93, Sweden 36, U.K. 16, Denmark 2, Switzerland 2, Canada 2, France 1, Argentine 1. An analysis by type of vaccination, injection number, and time interval, so far as such data are available, gives the following figures. Vaccine—pertussis alone, 28; pertussis + diphtheria, 17; triple, 67. Injection—first 48, second 36, third 18, fourth 3. Time interval—first day 78, second 10, third 5, fourth and thereafter 11.

Discussion

It must at once be said that it is impossible to adduce strictly scientific evidence that vaccination was the responsible factor in all the cases in my series, any more than in earlier publications. In individual cases another genesis is conceivable, due to the chance of circumstances. None the less, in no case can the possibility of association with vaccination be denied. The time relationship with vaccination is strongly suggestive; the symptoms conform to the findings of other authors; and the effects are very similar to those seen in the neurological sequelae to pertussis.

The possibility of simultaneous viral infection of the central nervous system has been suggested; but in Sweden the most common viruses which cause meningitis (polio, Coxsackie, E.C.H.O., Russian spring-summer encephalitis) never present such syndromes. Moreover, such reactions have not been reported after other vaccinations performed on a large scale—as, for instance, against diphtheria or poliomyelitis.

It may be assumed that the neurological complications after whooping-cough and after vaccination are provoked by the same agent, so that whether or not a reaction occurs might depend on the individual disposition. This assumption might encourage one to adopt the view that the child who reacts so powerfully to the vaccine would be the child who would also have developed neurological symptoms in whooping-cough. This is, to say the least, a dangerous line of thought, for it is unlikely that the sudden administration of a large dose of vaccine can be compared with the course of the natural infection—an infection which might in some cases have been mild. In this context it is of interest that Pittman (1951) showed that the sensibility of experimental animals to histamine may be greatly increased by pertussis vaccines. On inhalation of *H. pertussis* a similar sensibility occurred, but more slowly and of longer duration.

If the use of triple vaccination is to be continued its hazards should be appreciated and certain contraindications emphasized. Unfortunately the reaction often follows the first injection, so that it is not always possible to foresee whether a reaction will occur. The rapidity with which the reaction appears seems to suggest the possibility of a toxic or allergic factor. Berg (1958) mentions seven cases which exhibited accentuated reactions after repeated inoculations, and such cases are also included in our own series. Halpern and Halpern (1955) also suggest a certain caution with respect to children with a history of other allergic manifestations. Köng (1953) considers that familial neurological diseases, a history of convulsions, allergy, poor general health, and acute infections should all be regarded as contraindications. Berg (1958) and Cockburn (1959) state that continued vaccination is absolutely contraindicated in any suggestion of a neurological reaction to a previous pertussis inoculation. I imagine that we all must agree with these proposals.

In most countries whooping-cough is still a serious illness with an appreciable mortality risk. The W.H.O. statistics for 1955 show for 28 countries a mortality of 18 per million inhabitants per annum; in Sweden the rate was 1 per million. Only 65% of children in Stockholm develop clinical whooping-cough. Therefore the disease no longer imposes the burden on the family which it has done in the past.

In the light of these circumstances the attitude to vaccination cannot be the same in all countries. When there is a risk, and when the neurological complications may either be fatal or lead to serious consequences for the individual and the family, the situation needs to be reconsidered. Thus it may be questioned whether universal vaccination against pertussis is always justified, especially in view of the increasingly mild nature of the disease and of the very small mortality. I am doubtful of its merits at least in Sweden, and I imagine that the same question may arise in some other countries. We should also remember that the modern infant must receive a large number of injections and that a reduction in their number would be a manifest advantage.

Summary

In Sweden, as in several other countries, neurological complications after pertussis (triple) vaccination have been observed. A nation-wide investigation showed that 36 cases of such complications had occurred in about 215,000 vaccinated children (1 in 6,000) during 1955–8. Most of these consisted of convulsions, coma, or collapse, and the children were restored to health; but there were four deaths, of which two were sudden, and nine cases indicative of encephalopathies with severe lesions (1 in 17,000). An investigation of the incidence of neurological complications after pertussis showed that this was not so high as after vaccination. The increasingly mild nature of whooping-cough and the very low mortality in this disease in Sweden makes it questionable whether universal vaccination against it is justified. The same question may perhaps arise in some other countries.

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